

INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP2004/052029

A. CLASSIFICATION OF SUBJECT MATTER IPC 7 C07K14/705 G01N33/94 C12N5/10 C07D471/00 C07D513/00 C07D513/04 C07D279/18 A61K31/5415 A61K31/542		
According to International Patent Classification (IPC) or to both national classification and IPC		
B. FIELDS SEARCHED Minimum documentation searched (classification system followed by classification symbols) IPC 7 C07K G01N C07D A61K		
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched		
Electronic data base consulted during the international search (name of data base and, where practical, search terms used) EPO-Internal, BIOSIS, EMBASE, CHEM ABS Data, WPI Data, PAJ, Sequence Search		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	GREEN ANDREW ET AL: "Characterization of (3H)-CGP54626A binding to heterodimeric GABAB receptors stably expressed in mammalian cells" BRITISH JOURNAL OF PHARMACOLOGY, vol. 131, no. 8, December 2000 (2000-12), pages 1766-1774, XP001105031 ISSN: 0007-1188 the whole document	1-24
X	WISE A ET AL: "CALCIUM SENSING PROPERTIES OF THE GABAB RECEPTOR" NEUROPHARMACOLOGY, PERGAMON PRESS, OXFORD, GB, vol. 38, no. 11, November 1999 (1999-11), pages 1647-1656, XP000865720 ISSN: 0028-3908 the whole document	1-24
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<input checked="" type="checkbox"/> Further documents are listed in the continuation of box C. <input checked="" type="checkbox"/> Patent family members are listed in annex.		
* Special categories of cited documents : "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier document but published on or after the international filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art. "Z" document member of the same patent family		
Date of the actual completion of the international search 23 February 2005		Date of mailing of the international search report 24. 06. 2005
Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016		Authorized officer Valcarcel, R

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Box II Observations where certain claims were found unsearchable (Continuation of Item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of Item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☒ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☒ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-24

GABAB receptors having at least one GABABR1a and one GABABR2 subunit and methods involving said receptors
CHO cell line expressing hGABABR1a and hGABABR2, and methods for identifying GABAB agonists and antagonists involving the use of said cell line
Other methods to identify GABAB agonists and antagonists as defined in claims 9-12, 19, and 20

1.1. claims: 1-4,6-8

GABAB receptors having at least one GABABR1a and one GABABR2 subunit and methods involving said receptors

1.2. claims: 5,13-18,21-24

CHO cell line expressing hGABABR1a and hGABABR2, and methods for identifying GABAB agonists and antagonists involving the use of said cell line

1.3. claims: 9-12,19,20

Other methods to identify GABAB agonists and antagonists as defined in claims 9-12, 19, and 20

2. claims: 25-29

Compounds as defined in claim 27 (formula I), and use of compounds as defined in claims 25, 28 and 29 in the manufacture of medicaments

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	LANNEAU CHRISTOPHE ET AL: "Gabapentin is not a GABAB receptor agonist" NEUROPHARMACOLOGY, vol. 41, no. 8, December 2001 (2001-12), pages 965-975, XP001181057 ISSN: 0028-3908 the whole document	1-24
X	MARTIN AMANDA ET AL: "Pharmacological analysis of human GABAB (1a,2) and GABAB (1b,2) heterodimers expressed in CHO cells: Allosteric modulation of agonists and antagonists by Ca ²⁺ " BRITISH JOURNAL OF PHARMACOLOGY, vol. 129, no. Proceedings Supplement, January 2000 (2000-01), page 82P, XP009030031 Meeting of the British Pharmacological Society;Cambridge, England, UK; January 05-07, 2000 ISSN: 0007-1188 the whole document	1-24
X	WO 00/73788 A (MERCK FROSST CANADA INC ;NEIL GARY O (CA); NG GORDON (CA)) 7 December 2000 (2000-12-07) the whole document	1-24
X	CUI M ET AL: "IN VITRO CHARACTERIZATION OF GABAB RECEPTORS AND GABAPENTIN EFFECT." SOCIETY FOR NEUROSCIENCE ABSTRACT VIEWER AND ITINERARY PLANNER, vol. 2002, 2002, page Abstract No. 896.15, XP009029475 32nd Annual Meeting of the Society for Neuroscience;Orlando, Florida, USA; November 02-07, 2002 the whole document	1-24
X	NG GORDON Y K ET AL: "gamma-Aminobutyric acid type B receptors with specific heterodimer composition and postsynaptic actions in hippocampal neurons are targets of anticonvulsant gabapentin action" MOLECULAR PHARMACOLOGY, vol. 59, no. 1, January 2001 (2001-01), pages 144-152, XP002213218 ISSN: 0026-895X the whole document	1-24
X	WO 01/98779 A (MERCK FROSST CANADA INC ;NG GORDON (CA)) 27 December 2001 (2001-12-27) the whole document	1-24
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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	BRAEUNER-OSBORNE H ET AL: "FUNCTIONAL PHARMACOLOGY OF CLONED HETERODIMERIC GABAB RECEPTORS EXPRESSED IN MAMMALIAN CELLS" BRITISH JOURNAL OF PHARMACOLOGY, BASINGSTOKE, HANTS, GB, vol. 128, no. 7, December 1999 (1999-12), pages 1370-1374, XP000884864 ISSN: 0007-1188 the whole document	1-24
X	WO 99/51636 A (STORMANN THOMAS M ;BUSBY JAMES G (US); GARRETT JAMES E (US); NPS P) 14 October 1999 (1999-10-14) the whole document	1-24
X	US 6 465 213 B1 (EKSTRAND JONAS) 15 October 2002 (2002-10-15) the whole document	1-24
X	WO 99/40114 A (MERCK FROSST CANADA INC ;NG GORDON YIU KON (CA); BONNERT TIMOTHY P) 12 August 1999 (1999-08-12) the whole document	1-24
X	WO 00/14222 A (FRASER NEIL JAMES ;MARSHALL FIONA HAMILTON (GB); WISE ALAN (GB); G) 16 March 2000 (2000-03-16) the whole document	1-24
X	US 2002/045742 A1 (BOROWSKY BETH ET AL) 18 April 2002 (2002-04-18) the whole document	1-24
Y	KAUPMANN K ET AL: "HUMAN GAMMA-AMINOBUTYRIC ACID TYPE B RECEPTORS ARE DIFFERENTIALLY EXPRESSED AND REGULATE INWARDLY RECTIFYING K ⁺ CHANNELS" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA, NATIONAL ACADEMY OF SCIENCE. WASHINGTON, US, vol. 95, December 1998 (1998-12), pages 14991-14996, XP000867019 ISSN: 0027-8424 cited in the application the whole document	1-24

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Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WHITE J H ET AL: "HETERODIMERIZATION IS REQUIRED FOR THE FORMATION OF A FUNCTIONAL GABAB RECEPTOR" NATURE, MACMILLAN JOURNALS LTD. LONDON, GB, vol. 396, 17 December 1998 (1998-12-17), pages 679-682, XP000993024 ISSN: 0028-0836 cited in the application the whole document	1-24
X	----- HIRST WARREN D ET AL: "Pharmacological characterisation of a cell line expressing GABAB1b and GABAB2 receptor subunits." BIOCHEMICAL PHARMACOLOGY, vol. 65, no. 7, 1 April 2003 (2003-04-01), pages 1103-1113, XP001181103 ISSN: 0006-2952 the whole document	9-12,19, 20
Y	----- the whole document	1-24
X	WOOD M D ET AL: "The human GABAB1b and GABAB2 heterodimeric recombinant receptor shows low sensitivity to phaclofen and saclofen" BRITISH JOURNAL OF PHARMACOLOGY, vol. 131, no. 6, November 2000 (2000-11), pages 1050-1054, XP001180958 ISSN: 0007-1188 the whole document	9-12,19, 20
Y	----- the whole document	1-24
X	URWYLER STEPHAN ET AL: "Positive allosteric modulation of native and recombinant gamma-aminobutyric acidB receptors by 2,6-di-tert-butyl-4-(3-hydroxy-2,2-dimethyl-propyl)-phenol (CGP7930) and its aldehyde analog CGP13501" MOLECULAR PHARMACOLOGY, vol. 60, no. 5, November 2001 (2001-11), pages 963-971, XP001153169 ISSN: 0026-895X the whole document	9-12,19, 20
Y	----- the whole document	1-24
X	----- DATABASE CA [Online] CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; NEMERYUK, M. P. ET AL: "Synthesis and pharmacological activity of 4,9-diamino derivatives of 7,8-dihydro-1,3-diazaphenothiazine" XP002318964 retrieved from STN Database accession no. 1986:460576 abstract	25

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Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>& KHIMIKO-FARMATSEVTICHESKII ZHURNAL , 19(8), 964-8 CODEN: KHFZAN; ISSN: 0023-1134, 1985,</p> <p>-----</p> <p>DATABASE CA [Online] CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; NEMERYUK, M. P. ET AL: "4-Methoxy-7,8-dihydro-1,3-diazaphenthiazine amino derivatives and their neurotropic activity" XP002318965 retrieved from STN Database accession no. 1986:406472 abstract</p>	25
X	<p>& KHIMIKO-FARMATSEVTICHESKII ZHURNAL , 19(7), 810-14 CODEN: KHFZAN; ISSN: 0023-1134, 1985,</p> <p>-----</p> <p>DATABASE CA [Online] CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; POLEZHAEVA, A. I. ET AL: "Derivatives of dihydropyrimido[4,5-b][1,4]benzothiazine and their pharmacological properties" XP002318966 retrieved from STN Database accession no. 1982:85508 abstract</p>	25
A	<p>& KHIMIKO-FARMATSEVTICHESKII ZHURNAL , 15(11), 45-50 CODEN: KHFZAN; ISSN: 0023-1134, 1981,</p> <p>-----</p> <p>DATABASE CA [Online] CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; TYURINA, L. A. ET AL: "Algorithmic search for folic acid antagonists among the derivatives of pyrimido[4,5-b](1,4)benzothiazine" XP002318967 retrieved from STN Database accession no. 1986:454098 abstract</p>	25
	<p>& KHIMIKO-FARMATSEVTICHESKII ZHURNAL , 19(9), 1080-6 CODEN: KHFZAN; ISSN: 0023-1134, 1985,</p> <p>-----</p> <p>-/--</p>	

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DATABASE WPI Section Ch, Week 199410 Derwent Publications Ltd., London, GB; Class B02, AN 1994-081438 XP002318968 -& SU 811 776 A1 (A MED RADIOLOGY RES INST) 15 November 1993 (1993-11-15) abstract -----	25
X	WO 98/11885 A (ASTRA AKTIEBOLAG; ANDREWS, PAUL, L., R; LEHMANN, ANDERS) 26 March 1998 (1998-03-26) the whole document -----	25-29